

26. The method of Claim 20, comprising continuously applying the solution to the wound.

27. The method of Claim 26, comprising continuously irrigating the wound with the solution.

28. The method of Claim 20, wherein the solution is applied by irrigation of the wound.

29. The method of Claim 20, wherein the solution is locally applied to the wound in the absence of metabolic transformation.

30. The method of Claim 20, wherein the perioperative application of the solution comprises intraprocedural application together with preprocedural or postprocedural application of the solution.

31. The method of Claim 30, wherein the perioperative application of the solution comprises preprocedural, intraprocedural and postprocedural application of the solution.

32. The method of Claim 30, wherein the solution is continuously applied to the wound.

33. The method of Claim 20, wherein the soluble receptor in the solution is delivered locally at a concentration of no greater than 1,000 nanomolar.

34. The method of Claim 20, wherein the soluble receptor in the solution is included at a concentration or dosage that is sufficient to provide a level of inhibitory effect at the wound when delivered locally to the wound and that results in a plasma concentration that is less than a plasma concentration that would be required to achieve the same level of inhibitory effect at the wound when delivered systemically.

35. The method of Claim 25, wherein each of the additional agents in the solution is delivered locally at a concentration of no greater than 100,000 nanomolar.

36. The method of Claim 25, wherein each of the plurality of agents in the solution applied is included at a concentration or dosage that is sufficient to provide a level of inhibitory effect at the wound when delivered locally to the wound and that results in a plasma concentration that is less than a plasma concentration that would be required to achieve the same level of inhibitory effect at the wound when delivered systemically.

37. The method of Claim 25, wherein the at least one pain/inflammation inhibitory agent is selected from the group consisting of: serotonin receptor antagonists; serotonin receptor agonists; histamine receptor antagonists; bradykinin receptor antagonists; kallikrein inhibitors; tachykinin receptor antagonists including neurokinin<sub>1</sub> receptor subtype antagonists and neurokinin<sub>2</sub> receptor subtype antagonists; calcitonin gene-related peptide receptor antagonists; interleukin receptor antagonists; phospholipase inhibitors including PLA<sub>2</sub> isoform inhibitors and PLC<sub>γ</sub> isoform inhibitors; cyclooxygenase inhibitors; lipooxygenase inhibitors; prostanoid

*C1 cont*

receptor antagonists including eicosanoid EP-1 receptor subtype antagonists and eicosanoid EP-4 receptor subtype antagonists and thromboxane receptor subtype antagonists; leukotriene receptor antagonists including leukotriene B<sub>4</sub> receptor subtype antagonists and leukotriene D<sub>4</sub> receptor subtype antagonists; opioid receptor agonists including  $\mu$ -opioid receptor subtype agonists,  $\Lambda$ -opioid receptor subtype agonists, and P-opioid receptor subtype agonists; purinoceptor agonists and antagonists including P<sub>2Y</sub> receptor agonists and P<sub>2X</sub> receptor antagonists; and ATP-sensitive potassium channel openers.

38. The method of Claim 37, wherein the selected pain/inflammation inhibitory agents are delivered locally at a concentration of: 0.1 to 1000 nanomolar for soluble receptors; 0.1 to 10,000 nanomolar for serotonin receptor antagonists; 0.1 to 2,000 nanomolar for serotonin receptor agonists; 0.01 to 1,000 nanomolar for histamine receptor antagonists; 0.1 to 10,000 nanomolar for bradykinin receptor antagonists; 0.1 to 1,000 nanomolar for kallikrein inhibitors; 0.1 to 10,000 nanomolar for neurokinin<sub>1</sub> receptor subtype antagonists; 1.0 to 10,000 nanomolar for neurokinin<sub>2</sub> receptor subtype antagonists; 1 to 1,000 nanomolar for calcitonin gene-related peptide receptor antagonists; 1 to 1,000 nanomolar for interleukin receptor antagonists; 100 to 100,000 nanomolar for PLA<sub>2</sub> isoform inhibitors; 100 to 200,000 nanomolar for cyclooxygenase inhibitors; 100 to 10,000 nanomolar for lipoxygenase inhibitors; 100 to 10,000 nanomolar for eicosanoid EP-1 receptor subtype antagonists; 100 to 10,000 nanomolar for leukotriene B<sub>4</sub> receptor subtype antagonists; 0.1 to 500 nanomolar for  $\mu$ -opioid receptor subtype agonists; 0.1 to 500 nanomolar for  $\Lambda$ -opioid receptor subtype agonists; 0.1 to 500 nanomolar for P-opioid receptor subtype agonists; 100 to 100,000 nanomolar for purinoceptor antagonists; and 0.1 to 10,000 nanomolar for ATP-sensitive potassium channel openers.

*(1) cont*

39. A solution for use in the preemptive inhibition of pain and inflammation at a wound during a surgical procedure, comprising at least one soluble receptor in a liquid irrigation carrier, the soluble receptor being included at a concentration or in a dosage form that is sufficient to provide a level of inhibitory effect at the wound when delivered locally to the wound and that results in a plasma concentration that is less than a plasma concentration that would be required to achieve the same level of inhibitory effect at the wound when delivered systemically.

40. The solution of Claim 39, wherein the soluble receptor is selected from the groups of soluble receptors consisting of tumor necrosis factor (TNF) soluble receptors, interleukin-1 (IL-1) cytokine receptors, class I cytokine receptors, and receptor tyrosine kinases.

41. The solution of Claim 40, wherein the soluble receptor is selected from the groups of soluble receptors consisting of sTNFR, chimeric rhTNFR:Fc, human type I IL-1R, human type II IL-1R and shuman IL-1R fusion protein with DYKDDDDK on N-terminus.

42. The solution of Claim 39, wherein the soluble receptor is selected from the groups of soluble receptors consisting of soluble IL-2 receptor subfamily, soluble IL-6 cytokine receptor subfamily and fibroblast growth factor receptor family.

43. The solution of Claim 42, wherein the soluble receptor is selected from the group consisting of sIL-6R, bFGF receptor, PDGF and sFGFR.

44. The solution of Claim 39, which further comprises at least one additional pain/inflammation inhibitory agent selected to act on a different molecular target than the soluble receptor.

45. The solution of Claim 44, wherein the soluble receptor in the solution is included at a concentration of no greater than 1,000 nanomolar and each of the additional agents in the solution is included at a concentration of no greater than 100,000 nanomolar, adjusted for dilution in the absence of metabolic transformation, at an intended local delivery site.

46. The solution of Claim 44, wherein each of the plurality of agents in the solution is included at a concentration or dosage form that is sufficient to provide a level of inhibitory effect at the wound when delivered locally to the wound and that results in a plasma concentration that is less than a plasma concentration that would be required to achieve the same level of inhibitory effect at the wound when delivered systemically.

*Claim 47*  
47. The solution of Claim 44, wherein the at least one additional pain/inflammation inhibitory agents are selected from the group consisting of: serotonin receptor antagonists; serotonin receptor agonists; histamine receptor antagonists; bradykinin receptor antagonists; kallikrein inhibitors; tachykinin receptor antagonists including neurokinin<sub>1</sub> receptor subtype antagonists and neurokinin<sub>2</sub> receptor subtype antagonists; calcitonin gene-related peptide receptor antagonists; interleukin receptor antagonists; phospholipase inhibitors including PLA<sub>2</sub> isoform inhibitors and PLC<sub>γ</sub> isoform inhibitors; cyclooxygenase inhibitors; lipoxygenase inhibitors; prostanoid receptor antagonists including eicosanoid EP-1 receptor subtype antagonists and eicosanoid EP-4 receptor subtype antagonists and thromboxane receptor subtype antagonists; leukotriene receptor antagonists including leukotriene B<sub>4</sub> receptor subtype antagonists and leukotriene D<sub>4</sub> receptor subtype antagonists; opioid receptor agonists including μ-opioid receptor subtype agonists, Δ-opioid receptor subtype agonists, and P-opioid receptor subtype agonists; purinoceptor agonists and antagonists including P<sub>2Y</sub> receptor agonists and P<sub>2X</sub> receptor antagonists; and ATP-sensitive potassium channel openers.

48. The solution of Claim 47, wherein the additional pain/inflammation inhibitory agents are included at a concentration of: 0.1 to 10,000 nanomolar for serotonin receptor antagonists; 0.1 to 2,000 nanomolar for serotonin receptor agonists; 0.01 to 1,000 nanomolar for histamine receptor antagonists; 0.1 to 10,000 nanomolar for bradykinin receptor antagonists; 0.1 to 1,000 nanomolar for kallikrein inhibitors; 0.1 to 10,000 nanomolar for neurokinin<sub>1</sub> receptor

subtype antagonists; 1.0 to 10,000 nanomolar for neurokinin<sub>2</sub> receptor subtype antagonists; 1 to 1,000 nanomolar for calcitonin gene-related peptide receptor antagonists; 1 to 1,000 nanomolar for interleukin receptor antagonists; 100 to 100,000 nanomolar for PLA<sub>2</sub> isoform inhibitors; 100 to 200,000 nanomolar for cyclooxygenase inhibitors; 100 to 10,000 nanomolar for lipoxygenase inhibitors; 100 to 10,000 nanomolar for eicosanoid EP-1 receptor subtype antagonists; 100 to 10,000 nanomolar for leukotriene B<sub>4</sub> receptor subtype antagonists; 0.1 to 500 nanomolar for  $\mu$ -opioid receptor subtype agonists; 0.1 to 500 nanomolar for  $\Lambda$ -opioid receptor subtype agonists; 0.1 to 500 nanomolar for P-opioid receptor subtype agonists; 100 to 100,000 nanomolar for purinoceptor antagonists; and 0.1 to 10,000 nanomolar for ATP-sensitive potassium channel openers.

49. A solution for use in the preemptive inhibition of pain and inflammation at a wound during a surgical procedure, comprising at least one soluble receptor in a liquid carrier for perioperative application, the soluble receptor being included at a concentration or in a dosage form that is sufficient to provide a level of inhibitory effect at the wound when delivered locally to the wound and that results in a plasma concentration that is less than a plasma concentration that would be required to achieve the same level of inhibitory effect at the wound when delivered systemically.

50. A solution for use in the preemptive inhibition of pain and inflammation at a wound during a surgical procedure, comprising at least one soluble receptor and at least one additional agent that is an inhibitor of pain and/or inflammation in a liquid carrier, the soluble receptor and the at least one additional agent being selected to act on differing molecular targets and included at a concentration or in a dosage form that is sufficient to provide a level of inhibitory effect at the wound when delivered locally to the wound and that results in a plasma concentration that is less than a plasma concentration that would be required to achieve the same level of inhibitory effect at the wound when delivered systemically.